

WHAT IS CLAIMED IS:

1 1. A regulator comprising a material selected from the
2 group consisting of a protein, active fragments thereof,
3 agonists thereof, mimics thereof, and combinations thereof,
4 said regulator having the following structural character-
5 istics:

- 6 a) an N-terminal RING finger motif; and
7 b) a long coiled-coil domain comprising a C-terminal
8 subdomain characterized by a leucine-zipper.

1 2. The regulator of Claim 1 which is recruited by a
2 receptor selected from the group consisting of TNFR2 and
3 CD30.

1 3. The regulator of Claim 2 which is recruited by said
2 selected receptor via interaction with TRAF proteins.

1 4. The regulator of Claim 3 which is recruited by said
2 selected receptor via interaction with the TRAF2 homo-
3 oligomer.

1 5. The regulator of Claim 1 which is a polypeptide having
2 an amino acid sequence selected from the group consisting of
3 the full sequences shown in FIGURE 2A (SEQ ID NO: 1) (SEQ ID
4 NO: 2) and fragments thereof.

1 6. The regulator of Claim 1, wherein said coiled-coil
2 domain has an amino acid sequence selected from the group of
3 sequences consisting of residue numbers 56 through 275 shown
4 in FIGURE 2A (SEQ ID NO: 3) (SEQ ID NO: 4) and fragments
5 thereof exhibiting TRAF2 homo-oligomer specificity.

1 7. The regulator of Claim 1 which is derived from mammalian
2 cells.

1 8. The regulator of Claim 1 labeled with a detectable
2 label.

1 9. The regulator of Claim 8 wherein the label is selected
2 from the group consisting of enzymes, chemicals which
3 fluoresce and radioactive elements.

1 10. A DNA sequence or degenerate variant thereof, which
2 encodes TRIP or a fragment thereof, selected from the group
3 consisting of the nucleotide sequences shown in FIGURE 8 (SEQ
4 ID NO: 7) (SEQ ID NO: 8), DNA sequences that hybridize to any
5 of the foregoing DNA sequences under standard hybridization
6 conditions and DNA sequences that code on expression for an
7 amino acid sequence encoded by any of the foregoing DNA
8 sequences.

1 11. The DNA sequence of Claim 10, wherein said DNA sequence
2 is operatively linked to an expression control sequence.

1 12. A probe capable of screening for TRIP in alternate
2 species prepared from the DNA sequence of Claim 10.

1 13. A recombinant DNA molecule comprising a DNA sequence or
2 degenerate variant thereof, which encodes TRIP or a fragment
3 thereof, selected from the group consisting of the nucleotide
4 sequences shown in FIGURE 8 (SEQ ID NO: 7) (SEQ ID NO: 8),
5 DNA sequences that hybridize to any of the foregoing DNA
6 sequences under standard hybridization conditions and DNA

7 sequences that code on expression for an amino acid sequence
8 encoded by any of the foregoing DNA sequences.

1 14. A unicellular host transformed with a recombinant DNA
2 molecule comprising a DNA sequence or degenerate variant
3 thereof, which encodes TRIP or a fragment thereof, selected
4 from the group consisting of the nucleotide sequences shown
5 in FIGURE 8 (SEQ ID NO: 7) (SEQ ID NO: 8), DNA sequences that
6 hybridize to any of the foregoing DNA sequences under stand-
7 ard hybridization conditions and DNA sequences that code on
8 expression for an amino acid sequence encoded by any of the
9 foregoing DNA sequences.

1 15. A recombinant DNA molecule which upon transcription,
2 produces an antisense nucleic acid against TRIP mRNA,
3 said TRIP mRNA specific for translation of amino acid
4 sequences selected from the group consisting of amino acid
5 sequences shown in FIGURE 2A (SEQ ID NO: 1) (SEQ ID NO: 2)
6 (SEQ ID NO: 3) (SEQ ID NO: 4), FIGURE 2B (SEQ ID NO: 5) (SEQ
7 ID NO: 6) and fragments thereof,
8 said antisense nucleic acid comprising an nucleic acid
9 sequence capable of hybridizing to said TRIP mRNA.

1 16. The antisense nucleic acid of Claim 15, comprising said
2 nucleic acid sequence hybridizing to said TRIP mRNA for
3 interfering with said translation of said amino acid
4 sequences.

1 17. The antisense nucleic acid of Claim 15 which is RNA.

1 18. The antisense nucleic acid of Claim 15 which is DNA.

1 19. The antisense nucleic acid of Claim 15 which binds to
2 the initiation codon of said mRNA.

1 20. A method for detecting the presence or activity of TRIP,
2 said TRIP having a specificity for the TRAF2 homo-oligomer,
3 but not the TRAF2-TRAF1 hetero-oligomer, wherein said TRIP is
4 measured by:

5 A. contacting a biological sample from a mammal in
6 which the presence or activity of said TRIP is suspected with
7 said TRAF2 homo-oligomer under conditions that allow binding
8 of said TRIP to said TRAF2 homo-oligomer to occur; and

9 B. detecting whether binding has occurred between said
10 TRIP from said sample and TRAF2 homo-oligomer;
11 wherein the detection of binding indicates that presence
12 or activity of said TRIP in said sample.

1 21. A method of preventing cellular apoptosis in mammals,
2 comprising administering to a mammal a therapeutically
3 effective amount of an agent capable of inhibiting the
4 production of TRIP or a specific binding partner thereto,
5 said agent having the following characteristics:

6 a) is mediated by the receptor-TRAF2-TRAF1 complex;

7 b) has a specificity for the TRAF2-TRAF1 hetero-
8 oligomer; and

9 c) is a negative regulator of NF-kB activation.

1 22. A pharmaceutical composition for the treatment of
2 cellular debilitation, derangement and/or dysfunction in
3 mammals, comprising:

4 A. a therapeutically effective amount of a material
5 capable of inhibiting the production of TRIP, said material
6 being a negative regulator of NF-kB activation; and

7 B. a pharmaceutically acceptable carrier.

1 23. An antibody produced by injecting a substantially
2 immunocompetent host with an antibody-producing effective
3 amount of TRIP, active fragments thereof, agonists thereof,
4 mimics thereof, and combinations thereof, and harvesting said
5 antibody, said TRIP having an amino acid sequence selected
6 from the group consisting of the sequences delineated in
7 FIGURE 2A (SEQ ID NO: 1) (SEQ ID NO: 2) (SEQ ID NO: 3) (SEQ
8 ID NO: 4).

1 24. The antibody of Claim 23 labeled with a detectable
2 label.

1 25. The antibody of Claim 24 wherein the label is selected
2 from the group consisting of enzymes, chemicals which
3 fluoresce and radioactive elements.

1 26. The antibody of Claim 23 which is monoclonal.

1 27. The antibody of Claim 23 which is polyclonal.

1 28. A test kit for detecting the presence of TRIP in a
2 eukaryotic cellular sample, comprising:

3 A. a predetermined amount of a detectably labelled
4 specific binding partner to an amino sequence selected from
5 the group consisting of amino acid sequences shown in FIGURE
6 2A (SEQ ID NO: 1) (SEQ ID NO: 2) (SEQ ID NO: 3) (SEQ ID NO:
7 4), FIGURE 2B (SEQ ID NO: 5) (SEQ ID NO: 6) and fragments
8 thereof;

9 B. other reagents; and

10 C. directions for use of said kit.

1 29. The test kit of Claim 28 wherein said specific binding
2 partner is an immunochemically reactive component selected
3 from the group consisting of polyclonal antibodies, mono-
4 clonal antibodies and mixtures thereof.

1 30. The test kit of Claim 28 wherein said specific binding
2 partner is labelled with a label selected from the group
3 consisting of enzymes, chemicals which fluoresce and
4 radioactive elements.

1 31. A test kit for demonstrating the presence of TRIP in a
2 eukaryotic cellular sample, comprising:

3 A. a predetermined amount of anti-TRIP antibody
4 selected from Ab₁, Ab₂, a specific binding partner for TRIP
5 and combinations thereof;

6 B. other reagents; and

7 C. directions for use of said kit;

8 wherein either said anti-TRIP antibody is detectably
9 labelled.